BOOK REVIEWS

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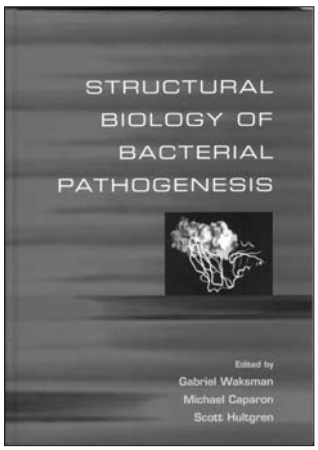

Structural biology of bacterial pathogenesis

GABRIEL WAKSMAN, MICHAEL CAPARON, SCOTT HULTGREN (EDS)

2005. ASM Press,
Washington DC, USA
273 pp, 18 × 26 cm
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Our understanding of bacterial pathogens has increased tremendously during the last several years. This has been mostly due to advances in molecular techniques, which allow a closer view of those strategies used by bacteria to cause disease. The twelve chapters of *Structural Biology of Bacterial Pathogenesis* review current knowledge on the structure of proteins involved in bacterial pathogenesis, either directly (such as adhesins or secretion machineries) or indirectly (regulatory factors, host primary defenses), although a discussion of most bacterial toxins has been deliberately excluded. The book also provides an inset of 52 color plates showing the structures of some of the proteins discussed in the text and providing models of protein–protein interactions, the assembly of macromolecular complexes, secretion machineries, etc.

The first two chapters are an overview of mechanisms by which bacterial pathogens sense and respond to environmental signals that trigger the expression of genes involved in pathogenesis. In the first chapter, the action of anti-sigma factors (proteins that interact with sigma factors, hence preventing the transcription of specific genes) is illustrated by three examples: regulation of sporulation in *Bacillus*, regulation of the periplasmic stress response, and regulation of the synthesis of bacterial flagella. Chapter 2 focuses on two-component systems, which consist of successful combinations of membrane-based histidine kinases and response regulators comprising highly effective signal transduction pathways. After reviewing the structural biology of both proteins, and more specifically those implicated in chemotaxis, the possibility of designing drugs targeting two-component systems is discussed.

The following two chapters focus on the structural biology of proteins involved in attachment and host cell recognition. Chapter 3 briefly describes the crystal structure of lectins located at the tip of diverse pili and fimbiae; such proteins mediate recognition of host cell carbohydrates. Chapter 4 reviews the sophisticated strategy used by enteropathogenic and enterohemorrhagic *Escherichia coli* strains. Each of these strains produces and injects into host cells a receptor for its own adhesin (called intimin). This allows the bacterium to attach to host cells strongly and independently of host-derived receptors, a strategy not found in any other bacterial pathogen.

The next set of chapters deals with bacterial mechanisms for secreting adhesins from the cytosol (in which they are produced) to the bacterial surface (where they will be displayed). In gram-negative bacteria, the chaperone–usher pathway (Chap. 5) consists of a periplasmic chaperone that folds and protects protein subunits, directing them to the point at which they will be assembled into pilus fibers. In Chap. 6, type IV pilus (i.e., *Vibrio cholerae* TCP, bundle-forming pilus of *E. coli* strains, etc.) are widely described in terms of the structure of pilin monomers, the structure of the pilus itself, and the contribution of other proteins that assist in pilus assembly. Finally, Chap. 7 reviews sortases, a large and ubiquitous family of proteins that covalently anchor surface proteins to the cell wall of gram-positive bacteria. Sortases are best exemplified by the *Staphylococcus aureus* SrtA transpeptidase.

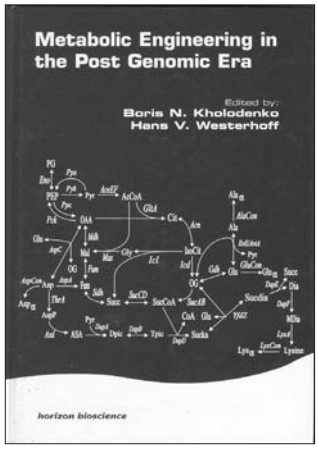
Haemophilus influenzae produces many adherence factors belonging to the type V secretion pathway; and their distribution among strains correlates with serotype. These adhesins are the subject of Chap. 8, in which crystal structures, the mechanism of secretion of monomeric and trimeric autotransporter proteins, and two-partner secretion pathways are detailed. Chapter 9 addresses type III secretion systems, which are shared by many gram-negative pathogens (such as *Salmonella* or *Pseudomonas* spp.) to deliver bacterial effector proteins directly to the host cell through a needle or syringe-like multiprotein complex. The bacterial effector proteins mimic host cell proteins, and so, they modulate the host cell cytoskeleton or interfere with host signal transduction pathways in order to ensure the success of the infection process. Type IV secretion systems (reviewed in Chap. 10) are structurally related to those of type III; however, type IV systems are involved in both the secretion of effector proteins into the host cell and the exchange of DNA through conjugation. These secretion systems were first discovered in *Agrobacterium tumefaciens*, and implicated in T-DNA trans-

fer to plant cells. Later, they were also found in pathogens such as *Bordetella pertussis*, *Brucella* spp., and *Helicobacter pylori*. Chapter 10 provides an extensive review of secretion systems of bacterial pathogens and a gene-to-gene description of the structure and function of every component. Returning to gram-positive bacteria in Chap. 11, the authors describe the *Streptococcus pyogenes* injectosome, which basically consists of toxins capable of forming oligomeric pores in the membrane of host cells (similarly to the effect of the listeriolysin toxin), then providing a way of entry for the effector proteins secreted through the Sec system.

Finally, Chap. 12 reviews the structure of Toll-like receptors in vertebrates. These receptors recognize specific pathogen-associated molecular patterns, thus providing a first-line defense (innate immune response) against microbial infection. The receptors can trigger a signal transduction cascade that is shared with that of interleukin-1 receptors (to which they also show structural similarity), with the activation of a transcription factor being the final event.

In summary, this book (which intends to be the first of a series of updates) provides extensive information on the structures and mechanism of proteins involved in bacterial pathogenesis. More importantly, for those readers not keen on highly detailed structural descriptions, it can also be read avoiding such discussions, while still transmitting an excellently updated overview of bacterial pathogenesis.

JOSÉ A. AÍNSA
Universidad de Zaragoza
ainsa@unizar.es



Metabolic engineering in the post genomic era

BORIS N. KHOLODENKO
HANS V. WESTERHOFF (EDS)

2004 Horizon Bioscience,
Norfolk, United Kingdom
456 pp, 15.6 × 23.4 cm
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In their attempts to control and direct living cells, bioengineers are confronted with enormous challenges, as the complexity of the existing hierarchy in living systems becomes apparent. *Metabolic Engineering in the Post Genomic Era*, deals with the most recent advances in the field of metabolic engineering. Starting from the first chapter, which briefly reviews the history of metabolic engineering, and continuing to the final chapter (Chap. 16), which poses and then answers several questions concerning situations that bioengineers face in the laboratory, the reader will continuously be surprised—as commented on the back cover—at the plasticity of living cells in their function as biological factories. This book aims to help the reader to understand and utilize the plasticity of the cell by reporting the most recent research results and by reviewing the major discoveries that have been made in this exciting field. The authors are internationally famous scientists in the field of metabolic engineering, and each has contributed a detailed discussion of his or her topic of interest.

The book has 16 well-structured chapters, each of which is accompanied by several schemes and tables that illustrate the concepts presented in the text. In the first chapter, after a brief review of the history of metabolic engineering, there is an attempt to change the reader's perception of the cell, substituting the notion that a cell is a component in the chain of production with the appreciation of the cell as a organism capable of production. The cell's plasticity provides it with a host of mechanisms that allow it not only to regulate itself, depending on external conditions, but also to avoid changes that are induced externally through engineering. The latter is accomplished by cellular homeostasis, which can inhibit attempts by engineers to introduce or modify specific cellular functions. Engineering modulates the metabolism of the cell, by regulating the expression of certain genes. Chapter 2

(Proteomics in metabolic engineering) describes the different approaches that are used to analyze the proteome. Although genome analysis has provided us with a wealth of knowledge about the many different forms of life, an understanding of its expressed form, i.e., the proteome, remains extraordinarily challenging, due to the many modifications and interactions that proteins undergo within the cell. Therefore, in order to effectively study the proteome, new techniques have been developed, such as 2D-electrophoresis, mass spectrometry, and protein arrays. Chapter 3 explains how phenotypic changes induced by deletions or mutations of unknown genes can be analyzed using magnetic resonance imaging and spectroscopy, which allow a thorough evaluation of the morphologic and metabolic consequences that occur following gene modification.

Chapter 4 deals with the necessity of developing tools that enable fast phenotypic characterizations of organisms whose genomes have been sequenced. Such tools allow rapid quantification of metabolic flow and are increasingly important in transmitting knowledge about the genotype into information about the phenotype. Chapter 5 discusses in depth the coordinated response of genes by means of a regulating network. Biochemical networks are commented on by examining the metabolic space, the protein space, and the genic space. With modern microarray technology, it is possible to measure the expression levels of thousands of genes, which provides insight into interactions between genes. Chapter 6 introduces the reader to MetaCyc, a database of metabolic pathways that describes 484 pathways and 1470 enzymes that occur in 167 organisms. MetaCyc provides an encyclopedic list of enzymes and their main characteristics, which allows researchers to find an enzyme whose characteristics can be exploited in metabolic engineering. Chapter 7 deals with experimental modulation of gene expression. The ability to modify enzymatic activities by changing the expression of the corresponding gene is a major tool for analyzing metabolic control, metabolic engineering, and metabolic optimization.

Chapter 8 offers an analysis of metabolic pathway in biotechnology and includes tables and illustrations that provide, e.g., simple examples of monosaccharide metabolism, such as the production of lysine in *Escherichia coli*. The chapter addresses the problem created by the overwhelming release of new genomic data, which have provided us with an enormous amount of sequence information that has not been accompanied by characterizations of the encoded enzymes. In Chap. 9 genotype-phenotype relationship is discussed using constraint-based models. Genome-scale models of the cellular metabolism of *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, and *Saccharomyces cerevisiae* have been constructed, and diverse constraint-based methods of cellular analysis are used to calculate the respective phenotypes. Chapter 10 describes a multi-scale approach to predictive modeling of metabolic regulation. Three sorts of data closely related to metabolic activity can be obtained: (i) the metabolic flows that can be determined experimentally with ^{13}C; (ii) intracellular concentrations of metabolites that can be measured by HPLC, enzymatic analyses, or LC-MS/MS; and (iii) enzymatic activities that can be determined from cellular extracts. All these data measure the stationary state of microorganisms under investigation. Although knowledge of metabolic flows is not sufficient to understand the regulation of the metabolic system, models based on the central metabolism of *Corynebacterium glutamicum* and the bacterium's biosynthesis of lysine have been constructed.

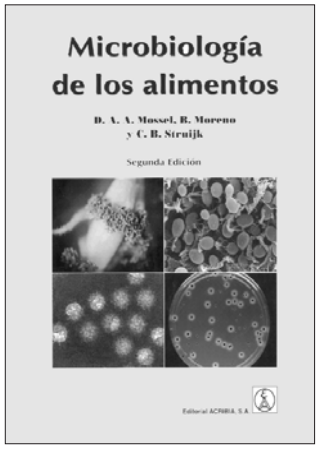
Chapter 11 is an introduction to the complex networks of intracellular reactions and a discussion of the search for an appropriate model to precisely predict dynamic intracellular behavior. In this respect, a general metabolic model together with illustrative examples of the kinetic activities of enzymes are presented. In order to describe enzyme kinetics, mathematical methods are required, as they simplify iterative models, analyses of sensitivity, valuation of parameters, calculations of the prediction, as well as selection of the correct model and experimental design. Chapter 12 discusses in depth the applications of bacterial whole cells in the pharmaceutical industry. *E. coli* is used as the microorganism of choice in experimental studies and to construct a mathematical model of metabolic and regulatory mechanisms. Construction of the model proceeds in four steps: (i) the function of proteins, genes, and their interactions should be determined; (ii) for each interaction, it is necessary to create a mathematical relation and then represent its kinetic equivalent; (iii) rate constants are determined by calibrating the model; (iv) all steps must be integrated into a coherent model. The construction of such models is used to understand the operation of the cell under the different situations that it may encounter, including during pharmaceutical applications.

Chapter 13 approaches secondary metabolic flows by means of coefficients that quantify the control of branch flows. Although the rates of the latter are proportional to the activities of their respective enzymes, the authors demonstrate that secondary flow may best be regulated by targeting enzymes in the primary metabolic pathway. The explanations are accompanied by detailed illustrations and they are pre-

sented experimentally in the case of pyruvate in the lactic acid bacterium *Lactococcus lactis*. Chapter 14 deals with the coordinated manipulation of multiple genes in metabolic engineering. In the last few years, new methods have appeared that have improved genetic manipulation while avoiding the disadvantages of previous methods, such as using single transgenes to target multiple genes. Chapter 15 addresses the synthesis of glycine betaine in plants and explains the routes by which this compound is produced and its applications. Glycine betaine increases resistance of the plant to osmotic strain (drought and salinity). Attempts to increase glycine betaine production have focused on the tobacco plant, and on the manipulation of genes that codify enzymes involved in the oxidation of choline and betaine aldehyde in the chloroplast. However, the results have demonstrated that there are limitations both in the import of choline from the cytosol to the chloroplast and in the endogenous synthesis of choline moieties. Metabolic modeling provides alternative strategies to improve glycine betaine overproduction. Chapter 16, which ends the book, is a discussion of the potential applications of metabolic engineering. In addition, answers to the questions raised in Chap. 1 provide a general conclusion to the subject matter.

Despite the many interesting topics discussed in *Metabolic Engineering in the Post Genomic Era*, this is a difficult book. Most chapters have lengthy explanations which are inadequately illustrated by the comparatively small number of diagrams, tables, and graphics. Due to their lack of previous knowledge and the specialized scientific terminology undergraduate students will find the topics covered in this book to be quite complicated. Instead, the book is clearly aimed at experienced scientists working in the fields of microbial and genetic or metabolic engineering.

ALFONSO LÓPEZ
INTERNATIONAL MICROBIOLOGY
alfons_lopez@hotmail.com



Microbiología de los alimentos, 2nd edn

D. A. A. MOSSEL, B. MORENO, C. B. STRUIJK (EDS)

2003. Editorial Acribia, Zaragoza, Spain
703 pp, 21 × 26 cm
Price: 75.00
ISBN 84-299-0998-9

Like the first edition, *Microbiologia de los alimentos* (2nd edn) fills a gap in the Spanish bibliography on food science and technology. While there are several very good texts dedicated to the chemical aspects of the field, only a few have focused on the microbiological ones. The didactic features of the book have been enhanced compared to the first edition: More figures and tables have been included, and the references have been modified, avoiding the most specialized and replacing them with reviews on the corresponding topic. Even so, the text preserves its rigorousness and takes note of all the novelties that have appeared in food science and technology during the last few years. Despite being visually unattractive, especially because its graphic content is poor and not very well-developed, the book can be a very useful reference. The vocabulary is easily understandable and the pleasant style of writing make the book easy to read. Moreover, adequate coverage of the topics allows the book to be quickly consulted, thereby providing a good source for daily work in the laboratory or simply as a bibliographic tool. *Microbiologia de los alimentos* was one of the last projects of Emeritus Professor David A. A. Mossel from the Medicine Veterinary Faculty at Utrecht University. Prof. Mossel died on August 30, 2004 (see Intl Microbiol 7:283-284, 2004). As a result of his productive scientific life, he was able to contribute several publications in the field of food microbiology and sanitation. He also participated in editing several books devoted to food microbiology, including this one.

The volume is divided into three parts. The first introduces the reader to the main microbiological concepts in the book. Part I contains information about the characteristics and taxonomy of food-borne bacteria and other microorganisms, including fungi and protozoa. It also describes the environmental conditions that are suitable for food-borne bacte-

rial development, and other factors that dynamically participate in the growth of microorganisms. Complete details of the metabolic activities of microorganisms on food and how these can be altered are provided. Possible diseases produced either by pathogenic microorganisms (from viruses to microscopic metazoan) or toxins generated by food microbiota are discussed. The last chapter of this part is devoted to the prevention of food contamination by microorganisms. In Part II of the book, the basis of control and evaluation of food manipulation are thoroughly discussed, including application of the practical information developed in the previous part. This second section comprises three chapters. The first "Prevention or microbiological security control and quality of food" deals with the general aspects and principles of security control and the different preservative methods. The second chapter focuses on the detection of microorganisms, toxins, and banned antimicrobial preservatives that may be present in food. The third chapter evaluates the efficiency of the previously described procedures with respect to their accuracy. The final part of the book gives a detailed description of the standard procedures and rules necessary to assess and monitor the manufacturing practices. This section introduces the reader to the application of an effective HACCP (hazard analysis critical control point) program for the food industry. This single chapter in Part III is subdivided into six subsections and serves as an industrial laboratory manual: The subsections are: (i) Introduction to laboratory good practices in microbiology; (ii) counting methods of microorganisms used as indicators; (iii) detection of infective and toxigenic microorganisms in processed food; (iv) counting of microorganism whose excess indicates food alteration; (v) Analysis of food implicated in cases of food poisoning; (vi) microbiological control of food processing areas.

Microbiologia de los alimentos is mainly a sound and complete compilation of the techniques and procedures applied in food microbiology. Although the latest molecular techniques are introduced, only 20 pages are devoted to them. While those methods probably are not currently used routinely for food microbiology analysis, they will be important in the future, so that a more detailed explanation of the molecular methods would have benefited the text. It is a comprehensive, specialized, and didactic book suitable for graduate students or undergraduates with an advanced knowledge of microbiology. In addition, it is a good tool for teaching and contains most of the topics developed in a food microbiology course. The accurate descriptions of all procedures and of HACCP allow the book to be used as a laboratory manual.

The industrial manufacture of food has become a general practice throughout the world. In order to control the safety of the food that we consume, it is necessary to develop and coordinate appropriate control measures and to ensure that the elaboration process and the final product conform with all sanitary regulations. This textbook provides the basis for understanding and improving the microbiological aspect of food science and technology and is a most convenient companion for researchers in this field.

JAVIER DEL CAMPO
University of Barcelona
delcampo@ub.edu